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AUTONOMIC AND RESPIRATORY RESPONSES OF SCHIZOPHRENIC AND NORMAL SUBJECTS TO CHANGES OF INTRA-PULMONARY ATMOSPHERE*

H. FREEMAN, M.D. AND E. H. RODNICK, Ph.D.**

THE AUTONOMIC nervous system of the schizophrenic patient has frequently been suspected of being much more sluggish in its activity than that of the normal individual. On the psychiatric level emotional blunting or slowness in response to situations that would normally demand some affective reaction, lack of interest, and indifference to environmental stimulation have been taken as clinical evidence of a gross behavioral sort in support of this impression.

Confirmatory indirect experimental evidence of the lesser reactivity of the autonomic nervous system of the schizophrenic subject is not lacking, although few studies have offered unambiguous evidence on this point. Most of these investigations have dealt with the vascular and metabolic responses to drug (*9*) or endocrine (*10*) preparations. The importance of such findings, however, indicates the necessity for a more direct approach to the problem. For this approach we have selected the heat regulating mechanisms.

This phase of reactivity was chosen primarily because it is mediated through the integrated autonomic nervous system, with the major center presumably in the hypothalamus (*17*). As autonomic responses are elicited most readily when the organism is placed under stress, the stress selected was the suppression of heat loss from the lungs by the inspiration of hot, moist oxygen. When this source of heat loss is blocked, other mechanisms must be evoked to establish a new level of compensation, else the organism is thrown into a phase of thermal dysequilibrium. Such compensatory reactions, therefore, serve as a measure of the degree of reactivity of the autonomic nervous system.

SUBJECTS AND PROCEDURE

The subjects included 31 normal and 29 healthy male schizophrenic patients. The non-psychotic control subjects were obtained from applicants for attendant positions in the hospital and were paid for their services. Their ages varied from 20 to 35, the average being just under 30. The schizophrenic subjects were selected at random from the Research Service ward of the hospital, the diagnosis having been established both by the hospital and the research staff. Their age range was approximately the same as that of the normal subjects. The only criterion for selection was good cooperation and at least moderate contact with the environment. The patients had been hospitalized for periods ranging from 2 months to 19 years, the average being 5.4 years. They represented, therefore, in the main a chronic stage of the psychosis and included all the recognized subtypes of schizophrenia. These consisted of 2 paranoids, 8 catatonics, 10 hebephrenics, 1 simple, and 8 individuals of an indeterminate type.

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** From the Research Service, Worcester State Hospital, Worcester, Mass.

The procedure consisted essentially in having the subject breathe oxygen through a mask connected with a Jones basal metabolism apparatus. For the first 10 minutes the inspired oxygen was kept at a temperature of approximately 30° C. and a relative humidity of approximately 20 per cent. The humidity was maintained at a low level by passing the oxygen through a desiccating chamber containing either calcium chloride or calcium sulfate. This initial ten minutes served to acclimate the subjects to the situation as well as to permit the measurement of the basal levels of the responses. At the end of this control period the oxygen was shunted by means of a valve, without the knowledge of the subject, through a chamber containing hot water in which it was heated to a temperature above that of the body and almost saturated with water vapor.

All tests were done in a non-basal state. The subjects, without clothing, reclined for about 15 minutes in a room in which the temperature was maintained at 30° C. and the relative humidity at 20 per cent, an environment in which heat production and heat loss were balanced (*12*). Thus, both the skin and the lungs during the control period were exposed to the same atmospheric condition.

A variety of autonomic responses were recorded each minute throughout the experimental session. The blood pressure was measured by means of a mercury manometer. The heart rate was read directly on the meter of a specially designed cardiotachometer (*13*). The palmar D.C. electrical resistance of the skin was measured by means of non-polarizable electrodes and a Wheatstone bridge arrangement, as described by Darrow (*3*). In this technique the active circular electrode ($\frac{7}{8}$ of an inch in diameter) was placed on the right palm while the larger inactive rectangular electrode ($3\frac{1}{2}$ by $2\frac{1}{4}$ inches in size) was placed on the medial aspect of the upper arm. The relatively non-polarizing electrodes consisted of a physiological zinc sulfate-kaolin paste

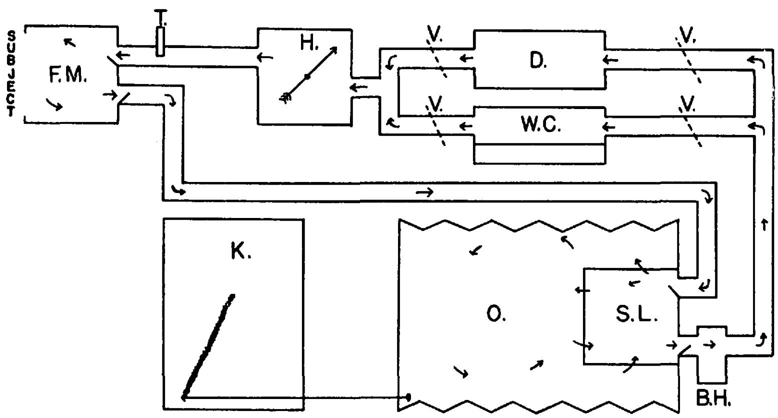

FIG. 1. Apparatus for varying temperature and humidity of inspired oxygen. The direction of oxygen flow is indicated by the arrows. K. = kymograph. O. = oxygen chamber of metabolism apparatus. S. L. = soda lime. B. H. = barium hydroxide solution. D. = drying chamber. W. C. = water chamber. H. = hygrometer. T. = thermometer. F. M. = face mask.

in metallic zinc cups. The active electrode was of "table" type, supported outside the area of electrical contact. The circuit suggested by Darrow has the special merit of keeping current comparatively constant at a low level of intensity. The rate and amplitude of respiration were obtained from the charts on the kymograph of the metabolism apparatus.

The experimental apparatus is shown schematically in *Fig. 1*. The entire system was kept air-tight. Various modifications of the original metabolism apparatus were necessitated by the exigencies of the experiment, such as placing an additional reservoir of oxygen in the input circuit and an extra cartridge of soda lime in the output system. The possibility of undue accumulation of carbon dioxide was checked by passing the oxygen over a 10 per cent solution of barium hydroxide. The relative humidity was measured by a hair hygrometer and the temperature by a small mercury thermometer placed just outside of the face mask in the tube carrying the inspired oxygen.

The discussion of the data will be confined to three readings in the control period, at the beginning (first minute), middle (fifth minute), and end (tenth minute) and to the level attained at the maximum temperature and humidity points.

In *Fig. 2* are shown the means of the temperature and relative humidity during the control period and the maximum elevation in the experimental period. In the control period the oxygen inspired by the normal subjects stayed at an average temperature of 29.7° C. For the patients the mean was 29.3° C. This variation is not considered to have any physiological significance. In the experimental period the temperature was increased to a maximum level for the normal subjects of 40.8° C. and for the patients to 41.0° C.[1]

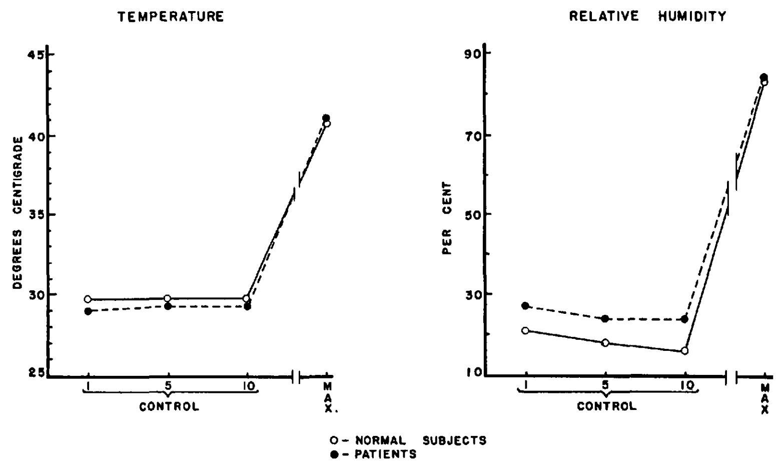

FIG. 2. Means of temperature and relative humidity of oxygen inspired by 31 normal subjects and 29 schizophrenic patients. The three control readings were taken at the first, fifth, and tenth minutes of the control period. The maximum reading represents the point at which the temperature and humidity were at a maximum.

[1] The rate and extent of the rise in temperature showed a fair amount of individual variation due both

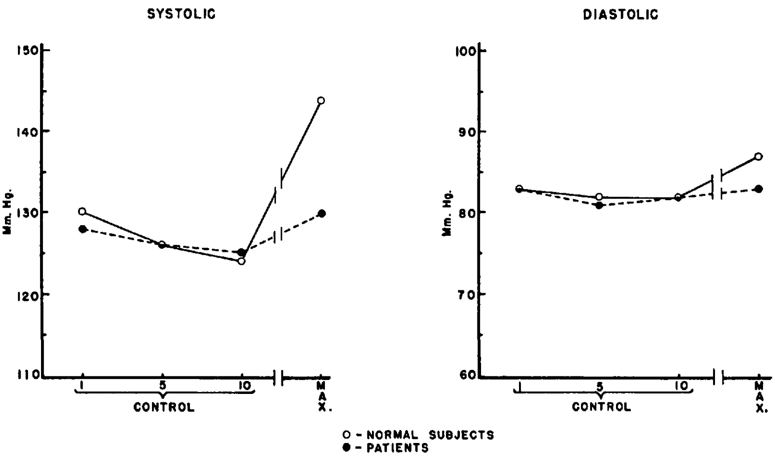

FIG. 3. Means of systolic and diastolic blood pressure values of 31 normal subjects and 29 schizophrenic patients. The three control readings were taken at the first, fifth, and tenth minutes of the control period. The maximum reading was taken at the point at which the temperature and humidity of the inspired oxygen were at a maximum.

The relative humidity of the inspired oxygen showed more variation in the control session than the temperature (*Fig. 2*). In the normal subjects it decreased from 20 per cent to 16 per cent whereas in the patients the values were consistently about 7 per cent higher. In the experimental period both values reached 83 per cent within three minutes after the oxygen passed through the water chamber.[2]

to difficulties inherent in the apparatus and to individual differences in the rate and amplitude of respiration. For the two groups of subjects, however, the rate of rise of temperature and the maximum height reached were quite similar. In the normal subjects it took 16.5 minutes to achieve this point and in the patients 15.5 minutes. Consequently we may conclude that a comparison between the two groups at this level of temperature is quite justified. The inspired oxygen was above body temperature rarely more than the last three minutes of the experiment.

[2] The actual level reached was undoubtedly one at which complete saturation occurred for water ran out of the hygrometer at the end of each experiment. The values in the control period are probably not entirely accurate and the difference between the normal and the psychotic subjects can be regarded as of little importance, especially in view of the fact that such a variation in humidity at this low level has little effect on temperature regulation.

RESULTS

Blood Pressure. The response of the blood pressure to the blocking of heat loss from the lungs is shown in *Fig. 3*. During the control period of 10 minutes the systolic blood pressure of the normal subjects fell from 130 mm. to 124 mm. while in the patients a lesser drop from 128 to 125 mm. is seen. These differences were found to have no statistical significance. It is interesting to note that both the normal and the psychotic subjects start at practically the same blood pressure level, indicating that there is no difference in tension between the two groups of subjects due to apprehension in the experimental situation. When the temperature and humidity of the inspired oxygen are raised, however, the systolic blood pressure of the normal controls rose 20 mm. from the last control reading to a level of 144 mm. The patients, on the other hand, showed a rise of only 5 mm. to a level of 130 mm. This difference between control and schizophrenic groups was found to have a "t" (7), based on stand-

ard deviations of 3.83. This represents a p (probability) of less than .01, and is highly significant

The diastolic pressures are at the same level in both groups (82 mm.) during the control session and show little change in the 10 minutes. In the experimental period, however, the normal subjects again display greater reactivity, the increase being 6 mm. as against 2 mm. for the patients. The difference between the groups has a "t" of only 1.28, however, and is not significant, the p being greater than .05.

Heart Rate. The graph of the mean heart rate response in *Fig. 4* shows a similar trend. The mean heart rate of the normal group rose from a level of 80 beats per minute at the end of the control period to a height of 106 beats at the end of the experiment—an increase of 26 beats per minute. During the corresponding period the mean increase for the patients is only 10 beats. The "t" of 4.15 for this difference of 16 beats per minute has a p of less than .01 and is hence highly significant. The lesser change in the patients cannot be attributed to their slightly lower initial level of 77 beats per minute, for no relationship was found between the initial level of heart rate and its maximum change. Furthermore, the difference of 3 beats between the two groups during the control period had no statistical significance.

Electrical Skin Resistance. The galvanic skin resistance showed the greatest variation of all the functions studied. Not only were there marked differences in the level of resistance among the various individuals but the direction of the trend under the experimental situation was less consistent. The normal subjects began at an average level of 9,000 ohms which was maintained at the fifth minute. After this the skin resistance fell to a level of 8,300. At the period of maximum temperature, the level decreased further to 6,700, a fall of 1,600 ohms from the last control reading. The patients started at a higher level of resistance (10,700 ohms) which increased during the con-

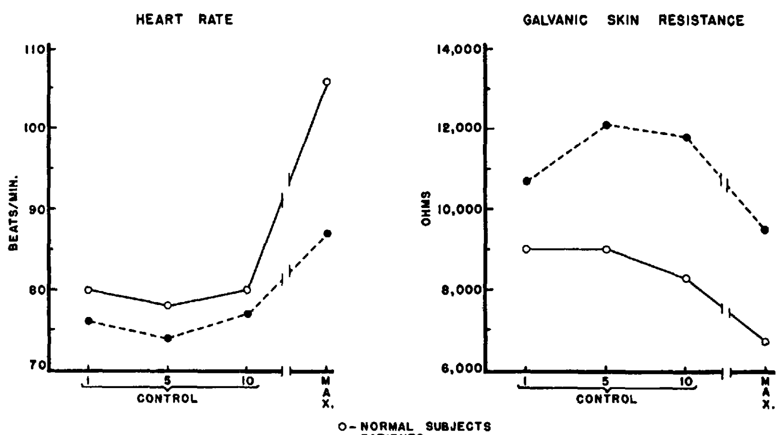

FIG. 4. Means of heart rate and galvanic skin resistance of 31 normal subjects and 29 schizophrenic patients. The three control readings were taken at the first, fifth, and tenth minutes of the control period. The maximum reading was taken at the point at which the temperature and humidity of the inspired oxygen were at a maximum.

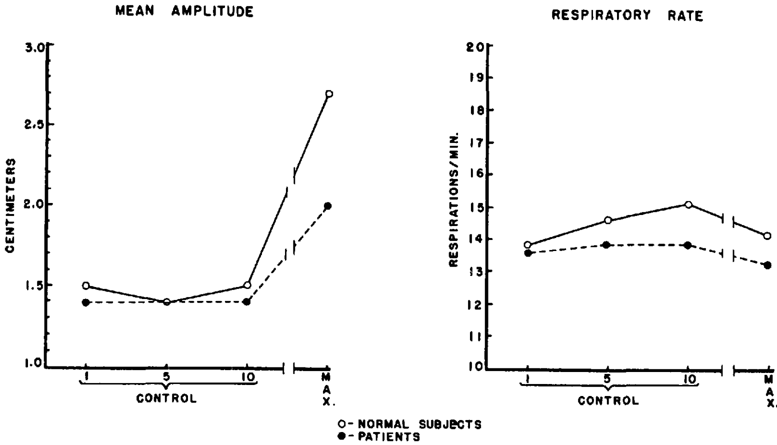

FIG. 5. Means of respiratory amplitude and rate in 27 normal subjects and 27 schizophrenic patients. The three control readings were taken at the first, fifth, and tenth minutes of the control period. The maximum reading was taken at the point at which the temperature and humidity of the inspired oxygen were at a maximum.

trol period to a level of 12,000 ohms. At 41° C. the resistance decreased 2,300 ohms. Although the change in resistance of the patients was absolutely greater than that of the normal subjects, the proportional drop from the last control reading was the same in both groups (19 per cent). The change in skin resistance from the last control reading to the point of maximum temperature and humidity was significant, although the difference between the schizophrenic patients and the normal controls was not. We are unable to draw any conclusions from this function except that the decrease in skin resistance indicated a definite autonomic reaction in both groups (*2, 5*).[3]

Respiration. The respiratory response to the intra-pulmonary heat stimulation shown in *Fig. 5*[4] is particularly interesting, especially in view of the fact that the respiratory mechanism was the one primarily affected by the experimental situation. The reaction manifested was quite consistent. The respirations tended to become more regular and somewhat slower in many cases. The amplitude of the individual respirations increased very markedly. The ordinate units of this figure represent the average amplitude of the individual respirations for each minute. As may be seen, the mean amplitude of respiration of the normal subjects rose from 1.5 cm. to 2.7 cm., an increase of 80 per cent. The increase in the corresponding period for the patients was only from 1.4 cm. to 2.0 cm., a change of 43 per cent. This significant difference of 37 per cent between the two groups has a "t" of 3.35 and a p of less than .01. While these figures give no information as to the actual respiratory volume, they are indicative of the change produced by the experimental situation.

The respiratory rate (*Fig. 5*) on the

[3] Converting the resistance units from ohms to conductance units (micromhs), as Darrow (*4*) recommends, makes no difference in the trend.

[4] The respiratory data are based on the findings of 27 subjects in each group since in the case of 4 normal subjects and 2 patients the kymographic apparatus went out of order during the experiment. This had no effect upon the recording of the other responses.

whole showed only slight change. In both normal controls and patients the high temperature caused a slowing of the rate of one respiration per minute.

This increase in respiratory amplitude accompanied by a slight slowing in rate is of some importance in the interpretation of the probable stimulus for the response pattern obtained. The possibilities of carbon dioxide excess in the apparatus or anoxemia resulting from a deficiency of oxygen are eliminated by the fact that there was no increase in the frequency of respirations (*14*, *19*). Checks on the apparatus during the experiment supported this conclusion. The effect was not due to thoracic muscular exertion resulting from resistance of the basal metabolism apparatus since respiratory fatigue is indicated by shallow and rapid breathing (*11*). Furthermore, there seems to be little indication that the effect resulted from a marked apprehension of the experimental conditions. The various varieties of respiratory reactions to emotion that have been reported, such as irregularity and increase in rate, do not seem to fit the picture obtained in this experiment (*6*). A similar syndrome of hyperpnoea, slight slowing of the respiratory rate, and air hunger was found by Landis *et al.* in subjects exposed to heat (*15*). The conclusion is thus reached that the particular physiological pattern here obtained is at least largely the result of the blocking of heat loss through the respiratory mechanisms. Additional evidence for this interpretation was found in an analysis of the individual cases. In 12 subjects there was at the close of the experiment a slight fall (1° C.) in the temperature of the inspired oxygen from the maximum. In 10 of these cases there was a corresponding decrease in the blood pressure, heart rate, and respiratory amplitude.

At the close of each session, each normal control subject was asked to give an introspective report of his reaction to the experimental procedure. The reports indicate that the most usual sensation was that the air became warm, moist, and somewhat stuffy, as on a humid summer day. In the case of 10 of the subjects there was a report of an increase in difficulty in breathing, although this did not occur until the very end of the experiment, when the temperature and humidity were close to the maximum. Three of the subjects indicated a sensation of dizziness at the time that the maximum temperature was reached. Eight subjects reported that they did not mind the stimulus in any way. Although these reports tend to indicate some discomfort toward the close of the experiment, when the temperature and humidity made the inspired oxygen very stuffy, yet it does not seem likely that apprehension toward the experimental situation could have been the basic variable involved in accounting for the marked sympathetic reaction obtained. In the first place, heart rate, blood pressure, and respiration began to show an effect considerably before the temperature had reached a maximum level, and definitely before the subjects indicated discomfort. Then again, the failure to find a reaction during the control period, or any difference in basal levels between schizophrenics and normals at that time, would seem to indicate that there was no difference in apprehension between the two groups of subjects. Furthermore, of the 22 subjects who registered some complaint of discomfort toward the close of the session, only 8 showed a systolic blood pressure rise that was greater than the mean of the entire group; 11 showed an increase in heart rate above the mean of the group; and only 10 showed an increase in tótal amplitude of respiration above the mean. A plotting of the distribution of the subjects who complained of the experimental procedure, or reported any

apprehension, showed that they were distributed randomly throughout the whole group of subjects; they were not necessarily the greater reactors.[5] It seems definite, therefore, that the rise in heart rate, blood pressure, and respiration amplitude could not be a result of mere apprehension alone to the experimental situation. Differences in apprehension and conscious awareness to the experimental situation cannot be the most important variable in accounting for the differences obtained between the normal and schizophrenic groups.

Psychiatric Rating vs. Autonomic Reactivity. In order to determine whether any relationship exists between degree of physiological reactivity and psychiatric status, each patient was ranked independently by a ward psychiatrist and the experimenters according to cooperation and contact with the environment. This rank order of the patients was then correlated in a scatter diagram with the increase in both heart rate and systolic blood pressure, as these were apparently the most reactive of the indicators used. There was no indication of any relationship between the degree of reactivity and psychiatric status as determined by our criteria. A similar lack of relationship existed for clinical subtypes and age of hospitalization. It is apparent, therefore, that degree of autonomic reactivity as measured in this experiment is independent of the clinical status of the patient once a chronic stage of the disorder has been reached. On the basis of these data, however, it is impossible to predict what relationships might be found in the more acute stage of the psychosis.

Discussion

Whether the factors underlying the present reaction be purely subcortical mechanisms, or an integration of the higher representation areas of autonomic functions such as may be involved on a cortical level, or whether they are tinged with the result of conscious responses as well, there is no question but that the schizophrenics respond less adequately than the normal subjects. It is important in this connection to point out that experiments on homeostasis do not indicate such striking differences between schizophrenics and normals under basal conditions (*8*, *9*). The differences appear only when a strong stress is placed upon the mechanism, sufficient to cause a marked autonomic reaction.

Since the experiment was designed to block off heat loss from the lungs, it might be expected, as a compensatory phenomenon, that the body temperature would rise. Experiences with diathermy, however, have shown that a minimum of 15 minutes is required before any rise in body temperature can occur, despite all precautions designed to prevent heat loss from the skin (*16*). Since in our situation all heat loss from the lungs is inhibited, a similarity in the trend of body temperature might be expected. In view of the fact, however, that the actual inhibition of heat loss from the lungs occurred for only the last few minutes of the experimental situation, not much change in body temperature could be expected, and hence this function was not measured. For this reason we utilized only rapid indicators of autonomic stress.

The "sluggishness" of adaptive functions observed in this experiment has been found to be a characteristic feature of schizophrenics in the chronic stage of the psychosis, not merely in the domain of heat regulation, but in other aspects of physiological and psychological function as well (*1*, *18*).

What relationship this abnormality of the homeostatic mechanisms has to the psychiatric disorder is as yet not

[5] The unreliability of introspective reports from schizophrenic subjects precludes a comparison with those of the normal subjects.

clear. One can only say that a deficiency in adaptive responsiveness of the autonomic reaction system might very well affect the ability of the schizophrenic patient to adjust in an efficient manner to the exigencies of the environment in which he is placed. Even when the stress of the environment is sufficiently strong to arouse an integrated autonomic reaction in normals, the schizophrenic is unable to respond adequately. The fact that the autonomic nervous system of the schizophrenic cannot react efficiently to strong stimulation might well militate against the merely sympathetic-stimulating effects of present therapeutic endeavors and might offer some explanation for the failure of such therapies in patients in the chronic stage of the psychosis.

Summary

The cardiovascular and respiratory reactions of 31 normal subjects and 29 schizophrenic patients have been studied in response to a thermal stress placed upon the organism by having them inspire oxygen in which the temperature was raised to 41° C. and the humidity to the saturation point. As indicators, the blood pressure, heart rate, galvanic skin resistance, and respiratory rate and amplitude were used.

Although the basal levels of the various indicators during a control period were quite comparable for both the normal controls and the patients, the control subjects gave significantly larger autonomic and respiratory responses to the increase in temperature and humidity of the inspired oxygen. The findings lend experimental support to indications that the schizophrenic patient is sluggish in adaptive reactivity of the autonomic nervous system.

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